RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)								DATE February 2000	
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense Wide/BA 3							R-1 ITEM NOMENCLATURE Medical Advanced Technology Program PE 0603002D8Z		
COST*(In Millions)*	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	Cost to Complete	Total Cost
Total Program Element (PE) Cost	2.109	1.996	2.043	2.075	2.115	2.154	2.200	Continuing	Continuing
Risk Assessment and Biamedical Applications/P506	2.109	1.996	2.043	2.075	2.115	2.154	2.200	Continuing	Continuing

(U) A. Mission Description and Budget Item Justification

(U) BRIEF DESCRIPTION OF ELEMENT

(U)This program supports efforts in advanced technology development to provide biomedical strategies for preventing, treating, assessing and predicting casualties from ionizing radiation, either alone or in combination with biological warfare (BW)/chemical warfare (CW) agents. It is directed at the need for the Department of Defense (DoD) to be prepared to execute military missions within radiation environments, to manage radiation crises associated with terrorist activities, and for consequence management in the event of nuclear weapons detonation. The DoD is ethically committed to protection of Service members from the adverse health effects of ionizing radiation to the fullest extent consistent with operational requirements. The program incorporates findings from basic and applied research into highly integrated and focused advanced technology development studies to produce: (1) protective and therapeutic strategies, (2) tools to measure radiation exposure to military personnel, and (3) accurate models to predict casualties, particularly in combined nuclear-biological-chemical (NBC) environments. The Armed Forces Radiobiology Research Institute (AFRRI), because of its multidisciplinary staff and exceptional laboratory and radiation facilities, is uniquely qualified to executes the program prescribed by its mission. Because national laboratories operated by the Department of Energy no longer support advanced research relevant to military medical radiobiology, AFRRI is currently the sole laboratory in existence with the combined capabilities needed to conduct this research.

RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2000
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense Wide/BA 3	**R-1 ITEM NOMENCLATURE** Medical Advanced Technology Program **PE 0603002D8Z**

COST*(In Millions)*	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	Cost to Complete	Total Cost
Total Program Element (PE) Cost	2.109	1.996	2.043	2.075	2.115	2.154	2.200	Continuing	Continuing
Risk Assessment and Biamedical Applications/P506	2.109	1.996	2.043	2.075	2.115	2.154	2.200	Continuing	Continuing

(U) Project Number and Title: P506 Risk Assessment and Biamedical Applications

(U) PROGRAM ACCOMPLISHMENTS AND PLANS

(U) FY1999 Accomplishments:

(U) Demonstrated broad spectrum radioprotective features of a non-toxic (non-androgenic) adrenocortical drug, 5-androstendiol (5-AED), compared to structurally similar analogs. ($ 0.148 Million)
(U) Demonstrated therapeutic benefit of combining two recombinant hematopoietic growth factors (IL-11 and G-CSF) into a single treatment protocol for acute radiation injury of the blood forming system.($ 0.168 Million)
(U) Completed initial studies to reduce the toxicity (nausea) associated with aminothiol prophylaxis through pro-drug modifying techniques.
($ 0.168 Million)
(U) Established *in vitro* radiation calibration curve for a simplified chromosome aberration measurement procedure in interphase cells. The procedure will facilitate fielding of chromosomal aberration assays to medical treatment facilities for rapid analysis of blood samples from mass casualties involving radiation exposures.
($ 0.369 Million)
(U)Further developed protocols for measuring molecular biomarkers (oncogene expression, mitochondria DNA deletions) with a compact, portable field-deployable platform. Established fluorogenic-5`-nuclease PCR primers and probes along with plasmid calibration standards for quantitative measurement of mitochondrial DNA mutations and ras proto-oncogene mRNA from cellular samples. This effort exploits the dual-use potential of a delivery platform under development elsewhere for military use that can rapidly measure and quantify nucleic acid changes by the polymerase chain reaction (PCR).
($ 0.304 Million)

RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2000
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense Wide/BA 3	**R-1 ITEM NOMENCLATURE** Medical Advanced Technology Program **PE 0603002D8Z**

(U) Developed prototype software tool to manage biodosimetric data under deployed field scenarios. Tool provides an integrated system for collecting, analyzing and tracking radiation exposures in individuals. Initiated *in vivo* validation studies under collaborative agreements and human-use protocols at clinical radiotherapy centers to validate precision and accuracy of newly developed biodosimetry systems in patients receiving radiotherapy.
($ 0.221 Million)
(U) Completed data reduction analysis on a segment of experimental data involving combined exposures to radiation and bacterial threat agents to enable incorporation into the Consequence Assessment Tool Set (CATS) for casualty rate predictions. The program will ultimately be capable of superimposing and analyzing radiation and BW footprints to produce a single output.
($ 0.321 Million)
(U) Filed patent applied for a simple method to detect uranium in bodily fluids that can be used to assess shrapnel casualties for DU fragments that may require surgical removal. Developed a method for rapid, simple identification of DU-containing metal fragments.
($ 0.410 Million)

(U) FY2000 Plans:

(U) Assess safety and radioprotective efficacy of the newly identified radioprotectant, 5-androstendiol, in a large, long-term pre-clinical animal study.
($ 0.300 Million)
(U) Assess toxicity and pharmacokinetics of second-generation slow-release prodrugs and drug capsule implants.
($ 0.176 Million)
(U) Continue *in vivo* studies validating chromosome aberration assay over a broad dose range and partial-body exposure situation. Test improved cytological analysis platforms using simple and easy-to-perform sample preparation protocols.
($ 0.347 Million)
(U) Complete initial-phase optimization of PCR-based assays for measuring multiple molecular biomarkers using field deployable platform. Analysis of multiple biomarkers using a single analysis platform provides enhanced and efficient diagnostic capability. Continue studies to validate screening assays for measuring radiation exposure.
($ 0.474 Million)
(U) Coordinate assembly of appropriate experimental data from *B. anthracis*/Rad animal studies and delivery to Defense Threat Reduction Agency`s Human Response Program for incorporation into the CATS program to model casualty predictions.
($ 0.303 Million)

RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2000
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense Wide/BA 3	**R-1 ITEM NOMENCLATURE** Medical Advanced Technology Program **PE 0603002D8Z**

(U) Complete development of method to measure uranium in urine of military personnel; provide protocol to application centers for assessment as a fieldable methodology. Complete development of protocols for a rapid, simple method to determine whether metal fragments contain DU. Based on results of ongoing AFRRI DU research, continue to contribute to revisions of fragment removal policies.
($ 0.400 Million)

(U) FY2001 Plans:

(U) Assess the added protective benefit of selectively combining non-toxic radioprotectants (e.g, 5-AED, plus Vitamin E) into a single pretreatment regimen by conducting a large, long-term preclinical animal study.
($ 0.310 Million)
(U) Assess safety and efficacy of the newly identified therapeutic cytokine combination, IL-11 plus G-CSF, in a large, long-term preclinical animal study.
($ 0.177 Million)
(U) Further validate biological marker assays for radiation exposure by determining their performance characteristics in measuring (1) exposure to gamma rays at low-dose rates and (2) in situations involving prior radiation exposures. The availability of a prior-exposure assessment capability is essential to permit dose assessment when analysis is delayed or when exposures are protracted.
($ 0.356 Million)
(U) Validate the automated imaging platform for radiation dose assessment. Continue validation of multiple molecular biomarker approach for diagnostic biodosimetric applications.
($ 0.486 Million)
(U) Provide recommendations to address any aberrations in *B. anthracis* vaccine efficacy as a consequence of exposure to ionizing radiation. Initiate efforts to incorporate performance-degrading consequences from combined radiation/bacterial and radiation/pyridostigmine exposures into casualty prediction models (CATS).
($ 0.310 Million)
(U) Complete patent application for rapid, simple DU fragment analysis method and provide fragment analysis protocol to application centers for their assessment of the procedure as a potential fieldable methodology. Based on results of ongoing AFRRI DU research, continue to contribute to revisions of fragment removal policies.
($ 0.404 Million)

RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2000
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense Wide/BA 3	R-1 ITEM NOMENCLATURE Medical Advanced Technology Program PE 0603002D8Z

(U) B. Program Change Summary	FY1999	FY2000	FY2001	Total Cost
Previous President's Budget	2.130	2.007	2.057	Continuing
Appropriated Value	0.000	0.000	0.000	Continuing
Adjustments to Appropriated Value				
a. Congressionally Directed Undistributed Reduction	(.021)	0.000	0.000	
b. Rescission/Below-threshold Reprogramming, Inflation Adjustment	0.000	(.011)	(.014)	
c. Other	0.000	0.000	0.000	
Current President's Budget	2.109	1.996	2.043	Continuing

Change Summary Explanation:

(U) **Funding:** Funding changes in FY 99 are due to congressional undistributed reductions. FY 2000 adjustments reflect inflation savings and the government wide rescission. FY 2001 reflects inflation savings.

(U) **Schedule:** N/A

(U) **Technical:** N/A

(U) **C.** **OTHER PROGRAM FUNDING SUMMARY COST:** N/A

(U) **D.** **ACQUISITION STRATEGY:** N/A

(U) **E.** **SCHEDULE PROFILE:** N/A